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=> s database and ((building blocks) or precursors) and combinatorial
         33119 DATABASE
         17689 DATABASES
         41700 DATABASE
                 (DATABASE OR DATABASES)
         94253 BUILDING
         14832 BUILDINGS
        102654 BUILDING
                 (BUILDING OR BUILDINGS)
         73693 BLOCKS
         10227 BUILDING BLOCKS
                 (BUILDING(W)BLOCKS)
         98632 PRECURSORS
         15525 COMBINATORIAL
             3 COMBINATORIALS
         15527 COMBINATORIAL
                 (COMBINATORIAL OR COMBINATORIALS)
L1          17 DATABASE AND ((BUILDING BLOCKS) OR PRECURSORS) AND COMBINATORIAL

=> d bib, abs 1-17
```

L1 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:301783 CAPLUS
TI Hierarchical protein folding pathways: A computational study of protein fragments
AU Haspel, Nurit; Tsai, Chung-Jung; Wolfson, Haim; Nussinov, Ruth
CS Sackler Institute of Molecular Medicine, Department of Human Genetics and Molecular Medicine, Sackler School of Medicine, Tel Aviv University, Tel Aviv-Jaffa, Israel
SO Proteins: Structure, Function, and Genetics (2003), 51(2), 203-215
CODEN: PSFGEY; ISSN: 0887-3585
PB Wiley-Liss, Inc.
DT Journal
LA English
AB We have previously presented a building block folding model. The model postulates that protein folding is a hierarchical top-down process. The basic unit from which a fold is constructed, referred to as a hydrophobic

folding unit, is the outcome of **combinatorial** assembly of a set of "**building blocks**." Results obtained by the computational cutting procedure yield fragments that are in agreement with those obtained exptl. by limited proteolysis. Here we show that as expected, proteins from the same family give very similar **building blocks**. However, different proteins can also give **building blocks** that are similar in structure. In such cases the **building blocks** differ in sequence; stability, contacts with other **building blocks**, and in their 3D locations in the protein structure. This result, which we have repeatedly obsd. in many cases, leads us to conclude that while a building block is influenced by its environment, nevertheless, it can be viewed as a stand-alone unit. For small-sized **building blocks** existing in multiple conformations, interactions with sister **building blocks** in the protein will increase the population time of the native conformer. With this conclusion in hand, it is possible to develop an algorithm that predicts the building block assignment of a protein sequence whose structure is unknown. Toward this goal, we have created sequentially nonredundant **databases** of building block sequences. A protein sequence can be aligned against these, in order to be matched to a set of potential **building blocks**.

RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:846117 CAPLUS
DN 138:237535
TI Software for automating analysis of encoded **combinatorial** libraries
AU Fitch, William L.; Zhang, Jing J.; Shah, Nikhil; Ouchi, Glenn I.; Wilgus, Robert L.; Muskal, Steven
CS Affymax Research Institute, Palo Alto, CA, 94304, USA
SO Combinatorial Chemistry and High Throughput Screening (2002), 5(7), 531-543
CODEN: CCHSFU; ISSN: 1386-2073
PB Bentham Science Publishers
DT Journal
LA English
AB The software applications that are used to automate the anal. of encoded **combinatorial** libraries are described. Com. packages from MDL, Oracle, and Agilent are linked with application software written in C/C++, in Microsoft Access and in ChemStation macro language. Encoding correspondence lists for each of up to three synthetic steps are conveniently assocd. with building block lists using the first application, CodeGen. The second application Decode allows the user to identify the individual beads picked onto a 96-well plate and the pool no. for each bead,. The decoding chromatog. data for each well is then loaded into the program. The chromatog. data is used to identify the tags used in the synthesis. Along with the building block information from ISIS/Host, the building block used in each step of the synthesis can be identified. A third routine, Code-to-Structure, takes the coded library **building blocks** and creates the connection table in ISIS for each structure found by the decode program. For quality control of encoded library synthesis, the decoded structures on a set of beads is compared to the LC/UV/MS data for the ligand cleaved from the same bead. CAPTURE, a GlaxoSmithKline proprietary application, is used to display and analyze the decoded structures and assocd. mass spectral data. This application uses simple isotopic compn. and electrospray ionization rule sets to predict mass spectra and judge the concordance of a structure-mass spectrum data set. An ancillary program, EIC, is used to ext. predicted single ion chromatograms from the full scan LC/MS data.

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:260946 CAPLUS
DN 135:13877
TI Scaffold architecture and pharmacophoric properties of natural products and trade drugs: application in the design of natural product-based **combinatorial** libraries
AU Lee, Man-Ling; Schneider, Gisbert
CS Pharmaceuticals Division, F. Hoffmann-La Roche Ltd., Basel, CH-4070, Switz.
SO Journal of Combinatorial Chemistry (2001), 3(3), 284-289
CODEN: JCCHFF; ISSN: 1520-4766
PB American Chemical Society
DT Journal
LA English
AB Natural products were analyzed to det. whether they contain appealing novel scaffold architectures for potential use in **combinatorial** chem. Ring systems were extd. and clustered on the basis of structural similarity. Several such potential scaffolds for **combinatorial** chem. were identified that are not present in current trade drugs. For one of these scaffolds a virtual **combinatorial** library was generated. Pharmacophoric properties of natural products, trade drugs, and the virtual **combinatorial** library were assessed using a self-organizing map. Obviously, current trade drugs and natural products have several topol. pharmacophore patterns in common. These features can be systematically explored with selected **combinatorial** libraries based on a combination of natural product-derived and synthetic mol. **building blocks**.
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:202053 CAPLUS
TI Computational and **combinatorial** chemistry-based approach to farnesyltransferase inhibitors
AU Park, Jewn Giew; Kollmeyer, Thomas M.; Xu, Kun; Prendergast, Franklyn G.; Pang, Yuan-Ping
CS Department of Molecular Pharmacology and Experimental Therapeutics, Mayo Foundation for Medical Education and Research, Rochester, MN, 55905, USA
SO Abstracts of Papers - American Chemical Society (2001), 221st, MEDI-153
CODEN: ACSRAL; ISSN: 0065-7727
PB American Chemical Society
DT Journal; Meeting Abstract
LA English
AB We have recently demonstrated the utility of in silico screening of chem. **databases** in identifying farnesyltransferase inhibitor leads. We have also demonstrated that dimerization of an enzyme inhibitor or its fragment can lead to analogs that are more potent than their parent compd. We further propose to use computers to identify a group of low mol. wt. mols. that can bind the active site of farnesyltransferase with micromolar affinity and use radiofrequency-encoded "split-and-pool" solid-phase synthesis to generate a directed library of dimers tethered by chem. chains. We report herein the in silico screening of chem. **databases** for effective **building blocks**, synthesis, and in vitro testing of a library of discrete compds. as farnesyltransferase inhibitors.

L1 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:133699 CAPLUS
DN 132:152086
TI Programmable one-pot oligosaccharide synthesis and structural effects of monosaccharides on the anomeric glycosylation reactivity
IN Wong, Chi-Huey; Zhang, Zhiyuan; Ollmann, Ian; Baasov, Timor; Ye, Xin-Shan
PA Scripps Research Institute, USA

SO PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000009527	A1	20000224	WO 1999-US18151	19990810
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2339639	AA	20000224	CA 1999-2339639	19990810
AU 9956720	A1	20000306	AU 1999-56720	19990810
EP 1104433	A1	20010606	EP 1999-943670	19990810
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002522598	T2	20020723	JP 2000-564977	19990810
US 6538117	B1	20030325	US 2001-762377	20010710
PRAI US 1998-96001P	P	19980810		
WO 1999-US18151	W	19990810		

AB The reactivity of a no. of p-methylphenyl thioglycoside (STol) donors which are either fully protected or have one hydroxyl group exposed has been quant. detd. by HPLC in conjunction with the development of a broadly applicable approach for a facile one-pot synthesis of oligosaccharides. The influence on reactivity of the structural effects of different monosaccharide cores and different protecting groups on each glycoside donor is characterized and quantified. In addn., a correlation between glycosyl donor reactivity and the chem. shift of the anomeric proton by 1H NMR has been established. A **database** of thioglycosides as glycosyl donors has been created using this reactivity data. The utility is demonstrated by the easy and rapid one-pot assembly of various linear and branched oligosaccharide structures. In addn., a computer program as been described for use as a **database** search tool and guide for the selection of **building blocks** for the one-pot assembly of a desired oligosaccharide or a library of individual oligosaccharides.
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:10975 CAPLUS
DN 132:146163
TI Color plates for this article are on pages 51-52. Molecular scaffold-based design and comparison of **combinatorial** libraries focused on the ATP-binding site of protein kinases
AU Stahura, Florence L.; Xue, Ling; Godden, Jeffrey W.; Bajorath, Jurgen
CS Computational Chemistry and Informatics, Bothell, WA, USA
SO Journal of Molecular Graphics & Modelling (1999), 17(1), 1-9
CODEN: JMGMFI; ISSN: 1093-3263
PB Elsevier Science Inc.
DT Journal
LA English
AB Compd. libraries were designed to target specifically the ATP cofactor-binding site in protein kinases by combining knowledge- and diversity-based design elements. A key aspect of the approach is the identification of mol. **building blocks** or scaffolds that are compatible with the binding site and therefore capture some aspects of target specificity. Scaffolds were selected on the basis of

docking calcns. and anal. of known inhibitors. We have generated 75 mol. scaffolds and applied different strategies to compute diverse compds. from scaffolds or, alternatively, to screen compd. **databases** for mols. contg. these scaffolds. The resulting libraries had a similar degree of mol. diversity, with at most 12% of the compds. being identical. However, their scaffold distributions differed significantly and a small no. of scaffolds dominated the majority of compds. in each library.

RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:668201 CAPLUS
DN 132:12061
TI Reactivity Prediction Models Applied to the Selection of Novel Candidate **Building Blocks** for High-Throughput Organic Synthesis of **Combinatorial** Libraries
AU Braban, Mircea; Pop, Iuliana; Willard, Xavier; Horvath, Dragos
CS CEREP, Lille, 59019, Fr.
SO Journal of Chemical Information and Computer Sciences (1999), 39(6), 1119-1127
CODEN: JCISD8; ISSN: 0095-2338
PB American Chemical Society
DT Journal
LA English
AB Quant. structure-property relationships (QSPRs) expressing the reactivity of compds. on the basis of mol. descriptors have been developed and applied to the computer-aided selection of synthons of appropriate reactivity for the high-throughput synthesis of **combinatorial** libraries. Our approach explicitly models the influence of substituents on the activity of the reactive center (RC), introducing specific mol. descriptors for their electronic, steric, and field effects (including the solvent effects) as a function of the 2D and 3D substituent-RC distances. Therefore, the approach requires a much smaller no. of empirical "substituent consts." than the classical Hammett approach. These consts. only depend on the chem. nature of the substituents and not on their relative position with respect to the RC. A general pKa prediction model was obtained by calibrating the weighting factors that express the relative influences of the electronic and field effect descriptors on the acidity of functional groups, using a learning set of about 500 org. amines and acids. A QSPR model expressing the degrees of conversion of a ref. amine in the amide synthesis reaction, in terms of the descriptors of the carboxylic acids, was then derived. The used learning set included 100 out of the 150 acids for which the conversions were exptl. detd. at the first stage of a typical selection process of **building blocks** for **combinatorial** synthesis. The predicted percentages of conversion of the acids not included in the learning set showed (abs.) errors not exceeding .+-.20%. As a consequence, this model is a useful computational tool in discriminating between reactive and inappropriate compds. from mol. **databases**, retrieving the **building blocks** that are most likely to comply with the reactivity criteria.

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:540370 CAPLUS
TI Virtual optimization of chemical libraries using genetic algorithm.
AU Pozzan, Alfonso; Leach, Andrew; Feriani, Aldo; Hann, Mike
CS Medicinal Chemistry Computational Chemistry, GlaxoWellcome S.p.A., 37135 Verona, 37135, Italy
SO Book of Abstracts, 218th ACS National Meeting, New Orleans, Aug. 22-26 (1999), CINF-004 Publisher: American Chemical Society, Washington, D. C.
CODEN: 67ZJA5
DT Conference; Meeting Abstract

LA English
AB One of the essential points in **combinatorial** library design concerns the selection of the monomers to be used as **building blocks** for the **combinatorial** synthesis of the final mols. Currently, public **databases** like the ACD consist of many thousands of mols. suitable as monomers to react under **combinatorial** chem. condition. Considering that the no. of available monomers is increasing and that **combinatorial** chem. technol. is giving access to more and more chem. reactions, one of the major tasks for library design is to select the best set of monomers out of a large no. of potentially reactants. For this reason we have developed in house a program called VOLGA (Virtual Optimization of chem. Libraries using Genetic Algorithm) which allowed us to optimize the design of a wide class of chem. libraries by choosing among different fitness functions.When VOLGA was planned, particular attention was paid to obtaining a program that could use any fitness function defined by the user. Fitness functions that have been successfully used to date include: 3D pharmacophore fitting, 2D similarity/dissimilarity measures, drug like profiles and QSAR derived models. The program allows optimization of libraries ranging from few tens up to 10000 mols. Optimization can be run by starting from potentially huge virtual libraries ranging from a few thousand to several millions mols. (i.e. All those that could be generated by **combinatorial** explosion of all the reactants considered in the design model). The aim of this paper is to critically analyze the different methods and scoring functions that have been used along with details on how classical GA theory was adapted in order to optimize **combinatorial** libraries. Advantages and drawbacks of this method are discussed.

L1 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:479630 CAPLUS
DN 131:266546
TI Virtual **Combinatorial** Syntheses and Computational Screening of New Potential Anti-Herpes Compounds
AU de Julian-Ortiz, Jesus V.; Galvez, Jorge; Munoz-Collado, Carlos; Garcia-Domenech, Ramon; Gimeno-Cardona, Concepcion
CS Unidad de Investigacion de Diseno de Farmacos y Conectividad Molecular Facultat de Farmacia and Departamento de Microbiologia, Hospital Clinico Universitario Facultat de Medicina Universitat de Valencia, Spain
SO Journal of Medicinal Chemistry (1999), 42(17), 3308-3314
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB The activity of new anti-HSV-1 chem. structures, designed by virtual **combinatorial** chem. synthesis and selected by a computational screening, is detd. by an in vitro assay. A virtual library of phenol esters and anilides was formed from two **databases** of **building blocks**: one with carbonyl fragments and the other contg. both substituted phenoxy and phenylamino fragments. The library of virtually assembled compds. was computationally screened, and those compds. which were selected by our math. model as active ones were finally synthesized and tested. Our antiviral activity model is a "tandem" of four linear functions of topol. graph-theor. descriptors. A given chem. structure was selected as active if it satisfies every discriminant equation in that model. The final result was that five new structures were selected, synthesized, and tested: all of them demonstrated activity, and three showed appreciable anti-HSV-1 activity, with IC50 values of 0.9 .mu.M. The same model, applied to a **database** of known compds., has identified the anti-herpes activity of the following compds.: 3,5-dimethyl-4-nitroisoxazole, nitrofurantoin, 1-(pyrrolidinocarbonylmethyl)piperazine, nebularine, cordycepin, adipic acid, thymidine, .alpha.-thymidine, inosine, 2,4-diamino-6-(hydroxymethyl)pteridine, 7-(carboxymethoxy)-4-methylcoumarin,

5-methylcytidine, and others that showed less activity.
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:401271 CAPLUS
DN 131:193734
TI Evaluation of PMF Scoring in Docking Weak Ligands to the FK506 Binding Protein
AU Muegge, Ingo; Martin, Yvonne C.; Hajduk, Philip J.; Fesik, Stephen W.
CS Pharmaceutical Products Division, Abbott Laboratories, Abbott Park, IL, 60064-3500, USA
SO Journal of Medicinal Chemistry (1999), 42(14), 2498-2503
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB A new knowledge-based scoring function (PMF-score), implemented into the DOCK4 program, was used to screen a **database** of 3247 small mols. for binding to the FK506 binding protein (FKBP). The computational ranking of these compds. was compared to the binding affinities measured by NMR. It was demonstrated that small, weakly binding mols. have, on av., higher computational scores than nonbinders and are enriched in the upper ranks of the computational scoring lists. In addn., the results obtained with the PMF scoring function were superior (by 30-120% larger enrichment factors) to those obtained with the std. force field score of DOCK4. The reliable ranking of small, weakly binding mols. offers new ways of designing **building blocks** in **combinatorial** libraries as well as SAR by NMR libraries with the increased chance of identifying suitable lead compds. for drug design.
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:29485 CAPLUS
DN 130:182673
TI Programmable One-Pot Oligosaccharide Synthesis
AU Zhang, Zhiyuan; Ollmann, Ian R.; Ye, Xin-Shan; Wischnat, Ralf; Baasov, Timor; Wong, Chi-Huey
CS Department of Chemistry and the Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SO Journal of the American Chemical Society (1999), 121(4), 734-753
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
AB In an effort to develop a broadly applicable approach to the facile one-pot synthesis of oligosaccharides, the reactivity of a no. of p-methylphenyl thioglycoside (STol) donors which are either fully protected or have one hydroxyl group exposed has been quant. detd. by HPLC. We have characterized and quantified the influence on reactivity of the structural effects of different monosaccharide cores and different protecting groups on each glycoside donor. In addn., we have established a correlation between glycosyl donor reactivity and the chem. shift of the anomeric proton by 1H NMR. Using the reactivity data, we have created a **database** of thioglycosides as glycosyl donors and demonstrated its utility in the easy and rapid one-pot assembly of various linear and branched oligosaccharide structures. In addn., we have developed the first computer program, OptiMer, for use as a **database** search tool and guide for the selection of **building blocks** for the one-pot assembly of a desired oligosaccharide or a library of individual oligosaccharides.
RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:268876 CAPLUS
DN 128:238882
TI RECAP-Retrosynthetic **Combinatorial** Analysis Procedure: A Powerful New Technique for Identifying Privileged Molecular Fragments with Useful Applications in **Combinatorial** Chemistry
AU Lewell, Xiao Qing; Judd, Duncan; Watson, Steve; Hann, Mike
CS Glaxo Wellcome Research and Development, Medicines Research Centre, Stevenage Hertfordshire, SG1 2NY, UK
SO Journal of Chemical Information and Computer Sciences (1998), 38(3), 511-522
CODEN: JCISD8; ISSN: 0095-2338
PB American Chemical Society
DT Journal
LA English
AB The use of **combinatorial** chem. for the generation of new lead mols. is now a well established strategy in the drug discovery process. Central to the use of **combinatorial** chem. is the design and availability of high quality **building blocks** which are likely to afford hits from the libraries that they generate. Herein the authors describe "RECAP" (Retrosynthetic **Combinatorial** Anal. Procedure), a new computational technique designed to address this building block issue. RECAP electronically fragments mols. based on chem. knowledge. When applied to **databases** of biol. active mols., this allows the identification of building block fragments rich in biol. recognized elements and privileged motifs and structures. This allows the design of **building blocks** and the synthesis of libraries rich in biol. motifs. Application of RECAP to the Derwent World Drug Index (WDI) and the mol. fragments/**building blocks** that this generates are discussed. The authors also describe a WDI fragment knowledge base which the authors have built which stores the drug motifs and mention its potential application in structure based drug design programs.
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:233957 CAPLUS
DN 129:150
TI Measuring molecular diversity: evaluation of alternative subsets selected from reagent building block libraries for **combinatorial** chemistry
AU Blankley, C. John
CS Parke-Davis Pharmaceutical Division, Department of Chemistry, Warner Lambert Company, Ann Arbor, MI, 48105, USA
SO Pharmacy and Pharmacology Communications (1998), 4(3), 139-146
CODEN: PPCOFN; ISSN: 1460-8081
PB Royal Pharmaceutical Society of Great Britain
DT Journal
LA English
AB There has been considerable interest recently in ways to measure and compare the diversity of collections of chem. compds., whether large **databases** of com. or proprietary origin, **combinatorial** libraries or functional group libraries of synthetic **building blocks**. This has been driven by technol. advances in **combinatorial** chem. synthesis and high throughput mass screening and the need to devise effective sampling techniques to identify information rich subsets or to inform decisions about **database** exchange or acquisition. Many useful statistical methods are available when the properties of mols. are the focus. If it is the diversity of the chem. structures themselves that is of interest, however, it is not so evident how to apply these methods. Mol. fingerprints, derived from connection tables, provide a mol. coding mechanism which lends itself to

quantitating similarity or, conversely dissimilarity or diversity of chem. structures. We have evaluated the use of different measures derived from mol. fingerprints for comparing datasets, and illustrate their performance in selecting diverse subsets from two libraries of reagent **building blocks** for **combinatorial** chem. applications. The compds. in the libraries were characterized in three distinctly different ways; a set of principal properties derived from conventional physicochem. descriptors; mol. fingerprints of two types; and by chem. space descriptors based on property-weighted connection tables. Alternative methods of diverse subset selection were also investigated. The results suggest that a single chem. description may not be suitable for all purposes, but that fingerprint-based descriptions can give reasonable diversity in traditional properties as well as topol. diversity. However, these are probably not suitable for quant. structure-activity relationship design purposes.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:141055 CAPLUS
TI RECAP-retrosynthetic **combinatorial** analysis procedure: A powerful new technique for identifying privileged molecular fragments with useful applications in **combinatorial** chemistry
AU Judd, Duncan B.; Lewell, Xiao Q.
CS Medicines Research Centre, Glaxo Wellcome Research and Development, Stevenage/Herts, SG1 2NY, UK
SO Book of Abstracts, 215th ACS National Meeting, Dallas, March 29-April 2 (1998), MEDI-023 Publisher: American Chemical Society, Washington, D. C. CODEN: 65QTAA
DT Conference; Meeting Abstract
LA English
AB RECAP is a powerful tool for identifying biol. privileged fragments for use in the synthesis of **combinatorial** libraries. The RECAP technique involves the use of **databases** of compds. with known biol. activity. These compds. are "cleaved" electronically at bonds amenable to **combinatorial** chem. The fragments and motifs can be readily used as **building blocks** to prep. **combinatorial** libraries rich in biol. priviledged substructural motifs. These libraries can be used for lead generation or lead optimization. The paper will discuss the principles of the technique and illustrate with a specific example.

L1 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:136066 CAPLUS
DN 128:153666
TI Developing an inhouse system to support **combinatorial** chemistry
AU Gobbi, Alberto; Poppinger, Dieter; Rohde, Bernhard
CS Novartis Crop Protection A.-G., Basel, CH-4002, Switz.
SO Perspectives in Drug Discovery and Design (1997), 7/8(Computational Methods for the Analysis of Molecular Diversity), 131-158 CODEN: PDDDEC; ISSN: 0928-2866
PB Kluwer Academic Publishers
DT Journal
LA English
AB To support the special data handling and design problems that arise in **combinatorial** chem., extensions to the classical chem. information and mol. design systems are required. In this article, the principles and the construction are described of a proprietary software system to support **combinatorial** chem., which was developed at Ciba-Geigy and is now used at Novartis. The system allows to register **combinatorial** libraries and their **building blocks**, as well as assocd. administrative information, assay results, and computed data. Structure similarity techniques are used to search through and to compare **combinatorial** libraries. The system can also be used to design

libraries manually or by computational selection of structurally diverse sets of **building blocks**.

L1 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:218651 CAPLUS
TI Ciclops - the ciba chemical library optimization system
AU Gobbi, A.; Poppinger, D.; Rohde, B.
CS Ciba Ltd., Basel, 4002, Switz.
SO Book of Abstracts, 211th ACS National Meeting, New Orleans, LA, March 24-28 (1996), CINF-060 Publisher: American Chemical Society, Washington, D. C.
CODEN: 62PIAJ
DT Conference; Meeting Abstract
LA English
AB We have developed a software system to support information handling and design aspects of working with **combinatorial** chem. libraries. The system uses PC Windows clients which access central **databases** for reagents, **building blocks**, and **combinatorial** libraries, as well as central computational services for design purposes. Server functionality is based on the Daylight **database** system. CICLOPS is interfaced to our existing inhouse **database** systems for handling screening data and corporate structures. The system supports manual and "rational" design of large mixt. and small discrete libraries, using methods pioneered by Chiron. It allows to compare the structural information content of **combinatorial** libraries. It also supports the logistics of CCL work (keeping track of reagents, library samples, deconvolution information). We will discuss software issues, our experiences with different methods for rational library design and for measuring library diversity, and how lab. chemists are using the system. We will also describe some ongoing work on how to design libraries to cover "holes" in existing compd. collections. This talk will discuss the information requirements related to the automated synthesis of mols. Topics include synthetic design, plate construction, anal. verification, and batch compd. registration. Interfaces for both computational and biol. screens are reviewed. The system is evolving, and as such has been designed to be modular, with components selected from a variety of vendors as well as custom components.

L1 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:218625 CAPLUS
TI Specific 3D **databases** as a tool to identify "mimetics".
AU Morize, I.; Guerin, V.; Luttmann, C.; James-Surcouf, E.
CS Med. Chem. Dept., CADD, Collegeville, PA, 19426, USA
SO Book of Abstracts, 211th ACS National Meeting, New Orleans, LA, March 24-28 (1996), CINF-034 Publisher: American Chemical Society, Washington, D. C.
CODEN: 62PIAJ
DT Conference; Meeting Abstract
LA English
AB 3D **database** searching techniques have recently proven to be a useful tool for new lead generation in the drug discovery process. On the other hand, the recent advances in robotics, miniaturization, and automation make possible simultaneous synthesis to produce libraries of org. compds. for biol. screening. In order to benefit from these two approaches in the drug discovery and optimization stages, we are currently developing new mol. modeling strategies in which some of the key features are: i) the generation of "specific 3D **databases**" gathering existing small mols. of a given type (ie. amino-acid like structures) and their use to identify constrained structures to be used in the modeling of peptidomimetics and subsequently to produce modified peptide libraries; ii) the diversity increase of fragment **database** used by De Novo program; iii) the generation of "**combinatorial** 3D **databases**" built by combining core structures (ie. a

building blocks or scaffolds) and sets of substituents and the use of 3D pharmacophore searching techniques. Procedure to identify scaffolds in corporate, or external, **database** and examples of specific 3D **database** generations will be presented and discussed with emphasis on modeling problems to be overcome when trying to mimic know active structures.